

Comparison of *In Vivo* and *In Vitro* Ocular Irritancy Classifications: Sorted by Reference

Substance Name	CASRN	<i>In Vitro</i> Conc. Tested	<i>In Vivo</i> Conc. Tested	Chemical Class	<i>In Vivo</i> Physical Form Tested	<i>In Vivo</i> (GHS) Classification ^{1,2}	<i>In Vivo</i> (EPA) Classification ^{3,4}	<i>In Vivo</i> (EU) Classification ^{5,6}	<i>In Vitro</i> Classification (IS(A)) ⁷	FHSA-20% ⁸	FHSA-67% ⁹	Reference
Triton X-100	9002-93-1	1%	1%	Ether	Solution	Nonirritant	Category III	Nonirritant	Severe	Irritant	Inconclusive	Bagley et al. (1992)
Oil/Water Emulsion-HZA		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Nonirritant	Irritant	Inconclusive	Gettings et al. (1994)
Oil/Water Emulsion-HZC		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Nonirritant	Irritant	Inconclusive	Gettings et al. (1994)
Oil/Water Emulsion-HZE		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Nonirritant	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZF		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Moderate	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZH		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Severe	Irritant	Irritant	Gettings et al. (1994)
Oil/Water Emulsion-HZI		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Slight	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZJ		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Nonirritant	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZL		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Slight	Irritant	Irritant	Gettings et al. (1994)
Oil/Water Emulsion-HZM		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Moderate	Irritant	Irritant	Gettings et al. (1994)
Oil/Water Emulsion-HZN		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Slight	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZO		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Nonirritant	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZR		Undiluted	Undiluted	Formulation	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Gettings et al. (1994)
Oil/Water Emulsion-HZS		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Severe	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZT		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Slight	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZU		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Nonirritant	Not labeled	Not labeled	Gettings et al. (1994)
Oil/Water Emulsion-HZV		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Nonirritant	Irritant	Inconclusive	Gettings et al. (1994)
Oil/Water Emulsion-HZW		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Nonirritant	Irritant	Irritant	Gettings et al. (1994)
Oil/Water Emulsion-HZY		Undiluted	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Severe	Not labeled	Not labeled	Gettings et al. (1994)
Surfactant Based Formulation 1-HZA		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 10-HZJ		10%	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Slight	Not labeled	Not labeled	Gettings et al. (1996)
Surfactant Based Formulation 11-HZK		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)

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Surfactant Based Formulation 12-HZL		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 13-HZM		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Slight	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 14-HZN		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 15-HZP		10%	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Slight	Irritant	Inconclusive	Gettings et al. (1996)
Surfactant Based Formulation 16-HZQ		10%	Undiluted	Formulation	Solution	Nonirritant	Category III	Nonirritant	Slight	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 17-HZR		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 18-HZS		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 19-HZT		10%	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Nonirritant	Not labeled	Not labeled	Gettings et al. (1996)
Surfactant Based Formulation 2-HZB		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Slight	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 20-HZU		10%	Undiluted	Formulation	Solution	Category 2B	Category III	R36	Slight	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 21-HZV		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 22-HZW		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 23-HZX		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 24-HZY		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 25-HZZ		10%	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Nonirritant	Not labeled	Not labeled	Gettings et al. (1996)
Surfactant Based Formulation 3-HZC		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 4-HZD		10%	Undiluted	Formulation	Solution	Category 2B	Category III	Nonirritant	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 5-HZE		10%	Undiluted	Formulation	Solution	SCNM	Category I	SCNM	Slight	Irritant	Inconclusive	Gettings et al. (1996)
Surfactant Based Formulation 6-HZF		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 7-HZG		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Moderate	Irritant	Irritant	Gettings et al. (1996)
Surfactant Based Formulation 8-HZH		10%	Undiluted	Formulation	Solution	Nonirritant	Category IV	Nonirritant	Slight	Not labeled	Not labeled	Gettings et al. (1996)
Surfactant Based Formulation 9-HZI		10%	Undiluted	Formulation	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Gettings et al. (1996)

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Acetic acid	64-19-7	10%	10%	Carboxylic acid	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Butanol	71-36-3	10%	10%	Alcohol	Solution	Category 1	SCNM	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Cetyltrimethylammonium bromide	57-09-0	10%	10%	Organic salt, Onium	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Chlorhexidine gluconate Solution (20% Solution)	18472-51-0	10%	10%	Amidine, Ester	Solution	Category 2B	Category II	Nonirritant	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Di(2-ethylhexyl) sodium sulfosuccinate	577-11-7	10%	10%	Organic salt, Sulfur containing compound, Ester	Solution	Category 1	Category I	R36	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Diisopropanolamine	110-97-4	10%	10%	Amine, Alcohol	Solution	Nonirritant	Category III	Nonirritant	Moderate	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Domiphen bromide	538-71-6	10%	10%	Organic salt, Onium, Ether	Solution	Category 1	Category I	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Ethanol	64-17-5	100%	100%	Alcohol	Liquid	SCNM	SCNM	SCNM	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Glycolic acid	79-14-1	10%	10%	Carboxylic acid, Alcohol	Solution	Category 2B	Category III	Nonirritant	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Lactic acid	50-21-5	10%	10%	Carboxylic acid, Alcohol	Solution	SCNM	Category III	SCNM	Severe	Irritant	Inconclusive	Hagino et al. (1999)/Submitted Y. Ohno Data
Lactic acid	50-21-5	100%	100%	Carboxylic acid, Alcohol	Liquid	Category 1	Category I	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Monoethanolamine	141-43-5	10%	10%	Amine, Alcohol	Solution	Category 2B	Category III	Nonirritant	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data
Triethanolamine	102-71-6	100%	100%	Amine, Alcohol	Liquid	Nonirritant	Category III	Nonirritant	Moderate	Irritant	Inconclusive	Hagino et al. (1999)/Submitted Y. Ohno Data

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Triethanolamine	102-71-6	10%	10%	Amine, Alcohol	Solution	Nonirritant	Category IV	Nonirritant	Severe	Not labeled	Not labeled	Hagino et al. (1999)/Submitted Y. Ohno Data/ Bagley et al. (1992)
Ethanol	64-17-5	10%	10%	Alcohol	Solution	Nonirritant	Category IV	Nonirritant	Slight	Not labeled	Not labeled	Hagino et al. (1999)/Submitted Y. Ohno Data/ Kojima et al. (1995)
Potassium laurate	10124-65-9	10%	10%	Organic salt, Carboxylic acid salt	Solution	Category I	Category I	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data/ Kojima et al. (1995)
Stearyltrimethylammonium chloride	15461-40-2	10%	10%	Organic salt, Onium	Solution	Category I	Category I	R41	Severe	Irritant	Irritant	Hagino et al. (1999)/Submitted Y. Ohno Data/ Kojima et al. (1995)
Sodium lauryl sulfate	151-21-3	10%		Organic salt, Carboxylic acid salt	Unknown	Category 1/Category 2A	Category I/Category II	R41/Nonirritant	Moderate	Irritant	Irritant	Kojima et al. (1995)
Triton X-100	9002-93-1	10%		Ether	Unknown	Category I	Category II	SCNM	Moderate	Irritant	Irritant	Kojima et al. (1995)

Abbreviations: CASRN = Chemical Abstracts Service Registry Number; Conc. = concentration; EPA = U.S. Environmental Protection Agency; EU = European Union; GHS = Globally Harmonized System; SCNM = study criteria not met.

¹ GHS=Globally Harmonized System (UN 2007)

² Eye Irritant Category I = irreversible effects on the eye/serious damage to the eye; Category 2A = reversible effects on the eye/irritating to the eyes; Category 2B = reversible effects on the eye/mildly irritating to the eyes; Nonirritant = not an eye irritant.

³ EPA=U.S. Environmental Protection Agency (EPA 2003a).

⁴ Toxicity Category I for the Primary Eye Irritation Study = Corrosive, or corneal involvement or irritation not reversible within 21 days; Category II = Corneal involvement or irritation clearing in 8-21 days; Category III = Corneal involvement or irritation clearing in 1-7 days; Category IV: minimal effects clearing in less than 24 hr

⁵ EU=European Union (EU 2001).

⁶ Risk phrase R41 = risk of serious damage to the eyes; R36 = irritating to the eyes; nonirritant = not an eye irritant.

⁷ IS(A) represents irritation scores that were calculated using the method described in Luepke (1985); classification scheme used as described in Luepke (1985).

⁸ FHSA=Federal Hazardous Substance Act (2005). FHSA-20% is based on the proportion of positive animals needed to identify a substance as an irritant using the FHSA sequential testing strategy, where 20% of the animals need to demonstrate a positive response for a substance to be identified as an irritant. A substance tested using 3 to 6 animals would not be labeled if $\leq 1/6$ animals were positive based on the FHSA criteria. The substance would be labeled as an irritant if there were ≥ 1 positive animal in a 3 to 5 animal test or ≥ 2 positive animals in a 6 animal test.

⁹ FHSA=Federal Hazardous Substances Act (2005). FHSA-67% is based on the proportion of positive animals needed to identify a substance as an irritant using the "first test" of the FHSA sequential testing strategy, where 67% of the animals need to demonstrate a positive response for a substance to be identified as an irritant. A substance tested using 3 to 6 animals would not be labeled if $\leq 1/6$ animals were positive based on the FHSA criteria. The substance would be labeled as an irritant if there were $\geq 2/3$, $3/4$, $4/5$, or $4/6$ positive animals. If $1/3$, $1/4$, $2/4$, $1/5$, $2/5$, $3/5$, $2/6$, or $3/6$ animals were positive, further testing would be required.